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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,204	10/19/2000	Janet A. Warrington	3240.1	7262

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EXAMINER

JOHANNSEN, DIANA B

ART UNIT PAPER NUMBER

1634

DATE MAILED: 08/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/693,204

Applicant(s)

WARRINGTON ET AL.

Examiner

Diana Johannsen

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

FINAL ACTION

1. This action is in response to paper no. 7, filed June 5, 2002. Claims 1-9 have been canceled, claims 10 and 12 have been amended, and claim 13 has been added. Claims 10-13 are now pending. The amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims. **This action is FINAL.**
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

**THE FOLLOWING ARE NEW GROUNDS OF OBJECTION NECESSITATED
BY APPLICANTS AMENDMENTS TO THE CLAIMS:**

3. Claims 10-13 are objected to because of the following informalities in claim 13. The claim includes a Markush group of names of "maintenance genes" that lacks proper punctuation. For example, several of the recited gene/protein names are not separated by commas (such that it appears that the claim may refer to a single gene rather than multiple genes)(e.g., "Adducin gamma subunit myosin regulatory light chain; Vacuolar ATP synthase subunit AC45 precursor ATP synthase gamma-subunit (L type).") Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. In view of the cancellation of claims 1-9, the rejection of the claims under 35 USC 112, second paragraph, is moot.

**THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED
BY APPLICANTS AMENDMENTS TO THE CLAIMS:**

5. Claims 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10-13 are indefinite over the recitation "comparing said expression of said gene in said plurality of samples using the expression of said at least three maintenance genes." First, the claim does not indicate with what "said expression of said gene in said plurality of samples" is to be compared. For example, are the samples to be compared with each other, with said maintenance genes, etc.? Second, the language "using the expression of said at least three maintenance genes" does not apprise one of skill in the art as to how "the expression of said at least three maintenance genes" is to be "used" in the comparing step of in the practice of the claimed method. Accordingly, it is unclear as to what comparisons are to be made and as to what actual steps must be taken to practice the method of the claims.

Claims 10-13 are indefinite over the recitation of the list of maintenance genes set forth in claim 13 (i.e., the recitation of "Profilin.....(VDAC)"). First, it is noted that the list appears to be a list of mRNA and protein names, rather than a list of gene names. Accordingly, it is unclear as to whether the claims are intended to require "measuring" of maintenance genes, or of proteins or mRNA molecules. Second, the list includes proteins having multiple subunits (e.g., ATP synthase), as well as some subunits included in those proteins (e.g., several ATP

synthase subunits are included in the recited list). Thus, it is unclear as to what molecules are encompassed by the claims. For example, may one detect any ATP synthase subunit/any gene encoding an ATP synthase subunit, or must one detect all, or only particular, ATP synthase subunits/genes? As the particular maintenance genes encompassed by the claims are unclear, the metes and bounds of the claims cannot be ascertained.

Claim Rejections - 35 USC § 102

6. In view of the cancellation of claim 9, the rejection of the claim under 35 USC 102(e) as being anticipated by MacLeod et al is moot.

7. In view of the amendment of claims 10-12 such that the claims depend from new claim 13 (rather than canceled claim 9), the rejection of claims 10-12 under 35 USC 102(e) as being anticipated by MacLeod et al is withdrawn.

Claim Rejections - 35 USC § 103

8. In view of the cancellation of claims 1-8, the rejection of the claim under 35 USC 103 as being unpatentable over MacLeod et al in view of Chen et al is moot.

**THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED
BY APPLICANTS AMENDMENTS TO THE CLAIMS:**

9. Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacLeod et al (U.S. Patent No. 6,221,600 B1 [4/2001; filed 10/8/1999]) in view of Kagawa et al (Int. J. Biochem. 20(3):219-29 [1990]).

It is first noted that the instant claims are not limited to, e.g., a particular set of "maintenance genes" with which unexpected results were



obtained, and that the claims as written are sufficiently broad so as to encompass the measuring of expression in any type of biological sample or samples and the "using" of "the expression of said at least three maintenance genes" in any manner. It is also noted that the specification discloses at pages 7-8 that "In this application, housekeeping genes are also referred to as maintenance genes."

MacLeod et al disclose methods in which a "set of genes is identified whose expression is relatively constant among different biological samples," which genes are "usually comprised of 'housekeeping' genes" (col 38, lines 35-46). MacLeod et al disclose the use of such sets of genes as "sets of control or standardization genes" in methods of monitoring and quantitating variations in gene expression among different tissue types (see entire reference). MacLeod et al disclose that expression of genes of interest is compared with expression of the set of standardization genes, and exemplify the calculation of expression ratios (see, e.g., col 38, lines 42-44, and Example 2). However, MacLeod et al do not disclose measuring at least three/five/ten of the maintenance genes recited in claim 13. Kagawa et al disclose the genes encoding ATP synthase are considered by those of skill in the art to constitute housekeeping genes (see entire reference, especially p. 219). Kagawa et al disclose that mammalian ATP synthase comprises 13 subunits (p. 220). Kagawa et al disclose that these subunits of ATP synthase are each encoded by a gene (see, e.g., p. 221), and it is a property of each of these genes that it constitutes a maintenance gene encompassed by the claims. Accordingly, Kagawa et al teach "at least ten

maintenance genes” that are encompassed by the instant claims as written. In view of the teachings of Kagawa et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of MacLeod et al so as to have employed therein a set of control genes including the group of housekeeping genes disclosed by Kagawa et al. While MacLeod et al exemplify a few particular sets of control genes, MacLeod et al indicate that those sets are “examples” (see col 38, lines 44-46), and MacLeod et al’s teachings encompass the use of sets of genes “whose expression is relatively constant among different biological samples,” which sets are “usually comprised of ‘housekeeping’ genes” (see col 38, lines 38-42). Accordingly, absent a showing of unexpected results with a particular set of known housekeeping genes, it would have been obvious to one of skill in the art to have employed any set of such genes – including a set comprising the housekeeping genes disclosed by Kagawa et al - as a control in the methods of MacLeod et al. An ordinary artisan would have been motivated to have employed the genes taught by Kagawa et al whenever those genes were readily available to the artisan, for the advantage of convenience.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

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Diana B. Johannsen
August 23, 2002



W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600